MILITARY MEDICINE, 180, 3:56, 2015

A Comparison of Acute Respiratory Distress Syndrome Outcomes Between Military and Civilian Burn Patients

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ABSTRACT Background: The objective of this report was to compare the prevalence of acute respiratory distress syndrome (ARDS) and associated mortality between military service members with burns sustained during or in support of combat operations and civilian burn patients treated at a single burn center. Methods*:* Demographic and physiologic data were collected retrospectively on mechanically ventilated military and civilian patients admitted to our burn intensive care unit between January 2003 and December 2011. Patients with ARDS were identified and categorized as mild, moderate, or severe using the Berlin criteria. Demographics and clinical outcomes were compared. After initial comparison, propensity matching was performed and mortality compared. Results*:* A total of 891 burn patients required mechanical ventilation during the study period; 291 military and 600 civilian. The prevalence of ARDS was 34% (n = 304) for the entire cohort, 33% (n = 96) for military, and 35% (n = 208) for civilians (p = 0.55). For the entire cohort, despite more severe injury burden, military patients had a significantly lower overall mortality (17% vs. 28%; p = 0.0002) as well as ARDS mortality (33 vs. 48%, p = 0.02) when compared to civilians. This difference was not significant after propensity matching based on age. Conclusion: In a retrospective cohort study, burned military patients on mechanical ventilation had a significantly lower overall and ARDS mortality despite larger burns and more severe injury when compared to civilian burn patients. This difference appears to be largely because of age.

INTRODUCTION

Development of acute respiratory distress syndrome (ARDS) is a common complication of burn injury and is associated with poor outcomes. Previous reports using the longstanding American-European Consensus Conference definition, show that between 40% and 54% of burn patients who require mechanical ventilation (MV) will develop ARDS.[1–3] These patients have a mortality between 14% and 42%.[1–3] Age, delayed resuscitation, sepsis, and inhalation injury (II) have been reported as risk factors for the development of ARDS.[1–5]

The Berlin definition for classifying ARDS defines three separate categories based on the degree of hypoxia measured as the ratio of partial pressure of arterial oxygen (PaO_2) to fraction of inspired oxygen (FiO_2)(PaO_2 to FiO_2 ratio [PFR]).[6] The three categories of the Berlin definition are (1) mild (200 mm Hg < PFR < 300 mm Hg), (2) moderate (100 mm Hg < PFR < 200 mm Hg), and (3) severe (PFR < 100 mm Hg) in the setting of at least 5 cm H_2O of positive end expiratory pressure.

The U.S. Army Institute of Surgical Research (USAISR) Burn Center serves as the sole referral center for all U.S. military burn casualties as well as the civilian regional burn center in South Texas. The USAISR's unique role in serving two distinct populations, allows for direct comparison of clinical outcomes. We have recently reported the application of the Berlin definition separately in a group of military burn patients, revealing that moderate and severe ARDS increased the odds of death by 4-fold and 9-fold, respectively.[7] In this article, we expand on this work by comparing ARDS-related outcomes among military burns to those of civilian burns admitted to our burn center. Differing baseline characteristics between civilian and military populations, as well as different mechanisms and patterns of burn injury, may impact the incidence and prognosis of ARDS between these two groups.

PATIENTS AND METHODS

Clinical Setting

The USAISR Burn Center is a Level V facility within an established chain of evacuation for U.S. combat causalties. Guidelines and protocols have been developed to ensure standardized prehospital resuscitation and care of burned combat casualties during evacuation.[8,9] There is a dedicated burn flight team capable of providing transcontinental evacuation of severely burned combat casualties to the USAISR. The USAIR also functions as the regional burn center in South Texas, serving a civilian population within an area of 80,000 square miles. All obtunded patients, patients with symptomatic II, and those at risk for airway compromise

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This article was presented at the Military Health System Research Symposium, Fort Lauderdale, Florida, August 14, 2013.

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doi: 10.7205/MILMED-D-14-00390

# Report Documentation Page	*Form Approved* *OMB No. 0704-0188*

1. REPORT DATE	2. REPORT TYPE	3. DATES COVERED
01 MAR 2015	**N/A**	**-**

4. TITLE AND SUBTITLE **A Comparison of Acute Respiratory Distress Syndrome Outcomes Between Military and Civilian Burn Patients**	5a. CONTRACT NUMBER 5b. GRANT NUMBER 5c. PROGRAM ELEMENT NUMBER
6. AUTHOR(S) **Waters A. J., Lundy J. B., Aden J. K., Sine C. R., Buel A. R., Henderson J. L., Stewart I. J., Cannon J. W., Batchinsky A., Cancio L. C., Chung K. K.,**	5d. PROJECT NUMBER 5e. TASK NUMBER 5f. WORK UNIT NUMBER
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) **United States Army Institute of Surgical Research, JBSA Fort Sam Houston, Tx 78234**	8. PERFORMING ORGANIZATION REPORT NUMBER
9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)	10. SPONSOR/MONITOR'S ACRONYM(S) 11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION/AVAILABILITY STATEMENT
Approved for public release, distribution unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

15. SUBJECT TERMS

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			
unclassified	**unclassified**	**unclassified**	**SAR**	**4**	

Standard Form 298 (Rev. 8-98)
Prescribed by ANSI Std Z39-18

are intubated during resuscitation and undergo fiberoptic bronchoscopy for evaluation of II.

Study Design and Participants

Approval for this study was obtained from the U.S. Army Medical Research and Materiel Command Institutional Review Board. All patients admitted to the USAISR requiring MV from January 2003 through December 2011 were included. Data collected from the electronic medical record included age, sex, height, weight, percentage of the total body surface area (TBSA) burned, percentage of full-thickness burn (FT), presence of II, injury severity score (ISS), and survival. Patients were included in the military cohort if they sustained their burns in support of or directly as a result of combat operations in Iraq or Afghanistan. The total volume of resuscitation fluid in the first 24 hours after injury, development of acute kidney injury (AKI) graded in accordance with the criteria of the AKI Network,[10] and blood products transfused before the diagnosis of ARDS were also examined. Three separate pulmonary critical care physicians (C.R.S., A.R.B., J. L.H.) reviewed records of patients included for evaluation to identify those meeting diagnostic criteria for ARDS based on the Berlin definition. Arterial blood gas values on the day of ARDS diagnosis were used to calculate PFR. For patients with ARDS, timing between injury and the diagnosis of ARDS was determined and recorded. Radiologic criteria were determined based on daily chest X-ray radiology reports. Heart failure or hydrostatic edema caused by fluid overload was ruled out based on echocardiography reports (subject to availability) or the evidence of improvement in pulmonary infiltrates with diuresis as the only intervention as documented in the daily progress notes. All patients that met the criteria for ARDS underwent a second chart review. In cases of disagreement, the senior author (K.K.C.) adjudicated.

Statistical Analysis

Continuous variables are reported as means ± standard deviation. Categorical variables are reported as proportions and, where appropriate, tested for significance using the χ^2 test. Stepwise logistic regression was performed to determine the independent variables most closely associated with moderate or severe ARDS. We then performed a propensity analysis matching the two groups by age and again compared all demographic and outcomes variables to include ARDS mortality (i.e., mortality among those with ARDS). All statistical analyses were completed using SAS version 9.2 (SAS Institute, Cary, North Carolina).

RESULTS

A total of 891 burn patients required MV during the study period; 291 military and 600 civilian. Table I illustrates and compares baseline demographic and outcomes data between these two groups overall. The military cohort was significantly younger than civilians (26 vs. 46 years, $p < 0.0001$) and was composed of a larger percentage of males (97% vs. 79%, $p < 0.0001$). The military cohort had a larger TBSA burned (34 vs. 28, $p = 0.002$), larger FT TBSA (26 vs. 13, $p = 0.002$), and a higher ISS (26 vs. 18, $p < 0.0001$). Additionally, II was significantly more common in military patients (45% vs. 35%, $p = 0.0004$) as was fresh frozen plasma (FFP) administration and pneumonia. Prevalence of ARDS was 34% for the entire cohort, and was no different for military (33%) when compared to civilians (35%). Overall mortality was lower in the military patients compared to civilians among all those in the study population (17% vs. 28%, $p = 0.0002$).

TABLE I. Comparison of Demographics and Outcomes Between Military and Civilian

	Military (n = 291)	Civilian (n = 600)	p Value
Age, Years	26 ± 7	46 ± 18	<0.0001
BMI	28 ± 6	28 ± 7	NS
Male (%)	97	79	<0.0001
ISS	26 ± 14	18 ± 14	<0.0001
TBSA (%)	34 ± 24	28 ± 24	0.002
II (%)	45	35	0.004
FT Burn (%)	26 ± 24	13 ± 21	0.002
FFP	1.62 ± 21	0.47 ± 21	0.0002
24-Hour Volume (L)	17.4 ± 12.8	11.7 ± 11.0	0.0002
AKI (%)	68	74	0.08
Pneumonia (%)	47	27	<0.0001
ARDS Overall (%)	33	35	NS
Mild (%)	6.2	5	NS
Moderate (%)	21	22	NS
Severe (%)	5.5	7.70	NS
Overall Mortality (%)	17	28	0.0002

AKI, acute kidney injury; ARDS, acute respiratory distress syndrome; BMI, body mass index; FFP, fresh frozen plasma; FT, full-thickness; II, inhalation Injury; ISS, Injury Severity Score; NS, Not Significant; TBSA, total burn surface area.

Table II depicts the demographic and outcomes data among just those with ARDS as a diagnosis per the Berlin criteria. The military cohort is still significantly younger. Although the TBSA is no longer different, ISS, FT, and II are higher in the military when compared to civilians. Additionally, military patients among those with ARDS appear to have received more FFP and more fluid (likely because of bigger burns), yet the mortality remains significantly lower.

Tables III and IV depict the variables that were significantly associated with the development of moderate or severe ARDS. Although II and FFP administration appeared to increase the odds of ARDS in the military group, these variables did not reach significance in the civilian group. Age was significantly associated with moderate and severe ARDS in the civilian cohort.

Propensity Matching

Table V depicts propensity matching based on 48 age matched pairs between the two cohorts among those with ARDS as a

TABLE II. Comparison of Demographics and Outcomes in Those With ARDS

	Military (n = 96)	Civilian (n = 208)	p Value
Age, Years	28 ± 9	51 ± 19	<0.0001
BMI	29 ± 5	28 ± 6	0.05
Male (%)	98	77	<0.0001
ISS	30 ± 15	22 ± 14	<0.0001
TBSA (%)	41 ± 26	35 ± 24	0.28
II (%)	56	43	0.03
FT Burn (%)	33 ± 26	16 ± 21	0.01
FFP	3 ± 7	1 ± 4	0.005
24-Hour Volume (L)[a]	20 ± 11	15 ± 12	0.03
AKI (%)	73	82	0.08
Pneumonia (%)	64	49	0.01
ARDS Mortality (%)	33	48	0.02

AKI, acute kidney injury; ARDS, acute respiratory distress syndrome; BMI, body mass index; FFP, fresh frozen plasma; FT, full-thickness; II, Inhalation Injury; ISS, Injury Severity Score; TBSA, total burn surface area. [a]Data available for 31 military patients.

TABLE III. Independent Variables Associated with Moderate or Severe ARDS in Military Burns

Independent Variable	OR	95% Wald Confidence Limits	p Value
II	1.90	1.01–3.54	0.046
ISS	1.04	1.01–1.07	0.0021
Pneumonia	1.98	1.07–3.66	0.03
FFP, Units	1.32	1.01–1.72	0.04

AKI, acute kidney injury; FFP, fresh frozen plasma; II, inhalation injury; ISS, Injury Severity Score.

TABLE IV. Independent Variables Associated With Moderate or Severe ARDS in Civilian Burns

Independent Variable	OR	95% Wald Confidence Limits	p Value
Age, Years	1.02	1.012–1.05	<0.0001
AKI	3.18	1.89–5.33	<0.0001
ISS	1.02	1.009–1.039	0.0012
Pneumonia	3.13	2.038–4.815	<0.0001

AKI, acute kidney injury; ISS, Injury Severity Score.

TABLE V. Propensity Matching by Age Only for Those With ARDS

	Military (n = 48)	Civilian (n = 48)	p Value
Age, Years	31 ± 10	31 ± 10	0.92
BMI	30 ± 6	28 ± 7	0.41
Male (%)	100	90	0.06
ISS	30 ± 15	28 ± 16	0.67
TBSA (%)	44 ± 26	43 ± 27	0.71
II (%)	55	56	0.96
FT Burn (%)	34 ± 26	22 ± 27	0.77
FFP	3 ± 7	2 ± 6	0.26
24-Hour Volume[a]	23 ± 12	18 ± 15	0.24
AKI (%)	73	79	0.47
Pneumonia (%)	63	48	0.15
ARDS Mortality (%)	33	38	0.67

AKI, acute kidney injury; ARDS, acute respiratory distress syndrome; BMI, body mass index; FFP, fresh frozen plasma; FT, full-thickness; II, inhalation injury; ISS, Injury Severity Score; TBSA, total burn surface area. [a]Data only available for 15 military patients.

diagnosis. In this analysis, mortality is no longer different between the two groups.

DISCUSSION

The main purpose of this study was to compare the prevalence of ARDS and its associated mortality in military service members with burns sustained during or in support of combat operations and civilian burn patients treated at a single burn center. One striking finding of this study is that, despite more severe injury defined by TBSA, FT, presence of II, and ISS, military patients had a significantly lower mortality. On logistic regression, II and FFP volume transfused were found to be predictive of moderate or severe ARDS exclusively in military patients, and age and AKI were unique to civilians. These predictors are consistent with a recent report from our institution utilizing the Berlin definition to assess prevalence and outcomes of ARDS in combat casualties[7] and emphasize the differences in these 2 populations reported on in this article. We have previously elucidated this difference by reporting that military burn patients have a higher ISS than their civilian counterparts and sustain injuries more frequently as a result of explosive mechanisms.[11] Prior reports from civilian literature have suggested that II is not predictive of the development of ARDS.[12] One possible explanation for our findings is that the inherent mean 96-hour evacuation time from injury to arrival at our center results in the deferment of burn center–specific treatment of II (frequent bronchoscopy and high-frequency percussive ventilation); therapy that is available immediately for civilians injured in close proximity to our facility.[8]

The results of propensity matching reveal that the significant mortality difference between the two cohorts did not persist when age is matched. Age as a risk factor for mortality is not unique to this report. The triad of age, TBSA, and presence of II remain the classic predictors of mortality in various models for thermal injury.[13–17] The earliest, widely used mortality predictive tool described in 1961 predicted mortality based on the sum of age and TBSA burned.[18] Since that time, various groups have reported the importance of II in other methods to predict mortality.[14,17] In a report describing the development of an age-specific predictive score of mortality, Moreau et al[19] described that the decrease in mortality reaches a nadir at age 21. Based on the significantly lower age and mortality of military, our outcomes are consistent with their findings.

The retrospective nature of this study carries with it certain inherent limitations. Even with detailed chart reviews, it can be difficult to make a diagnosis of ARDS with certainty.

There is a small subjective component to the diagnosis. Strict adherence to the Berlin diagnostic criteria and implementation of a structured adjudication process were used to overcome this limitation. The significant heterogeneous nature of the population made comparing outcomes difficult; this limitation was addressed by propensity matching. In addition, we are not able to take into account any other factor than age that may have contributed to the improved outcomes noted in military patients. The military population was almost exclusively male, whereas the civilian population was 75% male; this difference may have skewed the morality rates. There may be some inherent benefits to the physical training and nutrition that are inherent in military patients before injury and these were not able to be accounted for. However, as our propensity-matched results show, this is unlikely as BMI was no different between the two age-matched groups.

CONCLUSION

Among a burned population requiring MV, we found a significantly lower mortality in the military cohort when compared to civilians overall as well as in those with ARDS, despite more severe injury in the military group. However, this difference appears mostly because of age.

ACKNOWLEDGMENTS

K.K.C. contributed to the original conception of the study. S.M.B., A.R.B., C.R.S., I.J.S., and J.L.H. performed the data extraction and management. J.K.A., J.A.W., and K.K.C. performed the data analysis and created the charts and figures. J.A.W. and J. B. L. wrote the manuscript. I.J.S., J.W.C., A.B., L.C.C. and K.K.C. critically reviewed the manuscript. K.K.C. directed the study team and approved the final manuscript. Funding for this study was provided by the Clinical Trials for Burns and Trauma Task Area, U.S. Army Institute of Surgical Research.

REFERENCES

1. Dancey DR, Hayes J, Gomez M, et al: ARDS in patients with thermal injury. Intensive Care Med 1999; 25(11): 1231–6.
2. Liffner G, Bak Z, Reske A, Sjoberg F: Inhalation injury assessed by score does not contribute to the development of acute respiratory distress syndrome in burn victims. Burns 2005; 31(3): 263–8.
3. Fowler AA, Hamman RF, Good JT, et al: Adult respiratory distress syndrome: risk with common predispositions. Ann Intern Med 1983; 98(5 Pt 1): 593–7.
4. Hollingsed TC, Saffle JR, Barton RG, Craft WB, Morris SE: Etiology and consequences of respiratory failure in thermally injured patients. Am J Surg 1993; 166(6): 592–7.
5. Shirani KZ, Pruitt BA Jr, Mason AD Jr: The influence of inhalation injury and pneumonia on burn mortality. Ann Surg 1987; 205(1): 82–7.
6. Ranieri VM, Rubenfeld GD, Thompson BT, et al: Acute respiratory distress syndrome: the Berlin definition. JAMA 2012; 307(23): 2526–33.
7. Belenkiy SM, Buel AR, Cannon JW, et al: Acute respiratory distress syndrome in wartime military burns: application of the Berlin criteria. J Trauma Acute Care Surg 2014; 76(3): 821–7.
8. Renz EM, Cancio LC, Barillo DJ, et al: Long range transport of war-related burn casualties. J Trauma 2008; 64(Suppl 2): S136–S145.
9. CENTCOM Joint Theater Trauma System. Burn Care Clinical Practice Guideline. 2012. Available at http://www.usaisr.amedd.army.mil/clinical_practice_guidelines.html; accessed July 15, 2014.
10. Mehta RL, Kellum JA, Shah SV, et al: Acute kidney injury network: report of an initiative to improve outcomes in acute kidney injury. Crit Care 2007; 11(2): R31.
11. Kauvar DS, Leopoldo CC, Wolf SE, et al: Comparison of combat and non-combat burns from ongoing U.S. military operations. J Surgical Research 2006; 132: 195–200.
12. Liffner G, Bak Z, Reske A, Sjoberg F: Inhalation injury assessed by score does not contribute to the development of acute respiratory distress syndrome in burn victims. Burns 2005; 31: 263–8.
13. Santaniello JM, Luchette FA, Esposito TJ, et al: Ten year experiences of burn, trauma, and combined burn/trauma injuries comparing outcomes. J Trauma 2004; 57: 696–701.
14. Smith DL, Cairns BA, Ramadan F, et al: Effect of inhalation injury, burn size, and age on mortality: a study of 1447 consecutive burn patients. J Trauma 1994; 37: 655–9.
15. Ryan CM, Schoenfeld DA, Thorpe WP, et al: Objective estimates of the probability of death from burn injuries. N Engl J Med 1998; 338: 362–6.
16. Osler T, Glance LG, Hosmer DW: Simplified estimates of the probability of death after burn injuries: extending and updating the Baux score. J Trauma 2010; 68: 690–7.
17. Colohan SM: Predicting prognosis in thermal burns with associated inhalation injury: a systematic review of prognostic factors in adult burn victims. J Burn Care Res 2010; 31: 529–39.
18. Baux S: Contribution a l'Etude du traitement local des brulures thermigues etendues. Paris: These; 1961.
19. Moreau AR, Westfall PH, Cancio LC, Mason AD Jr: Development and validation of an age-risk score for mortality prediction after thermal injury. J Trauma 2005; 58: 967–72.